



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification <sup>6</sup> : C07H 21/04, C12N 1/21, 5/16, 15/12, 15/63, C07K 14/00, C12P 21/00, G01N 33/566</p>	<p>A1</p>	<p>(11) International Publication Number: <b>WO 97/25340</b></p> <p>(43) International Publication Date: 17 July 1997 (17.07.97)</p>
<p>(21) International Application Number: PCT/US96/00499</p> <p>(22) International Filing Date: 11 January 1996 (11.01.96)</p> <p>(71) Applicant: HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850-3338 (US).</p> <p>(72) Inventor: LI, Yi; 16125 Howard Landing Drive, Gaithersburg, MD 20878 (US).</p> <p>(74) Agent: BENSON, Robert, H.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US).</p>		<p>(81) Designated States: AU, CA, CN, JP, KR, MX, NZ, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p><b>Published</b> <i>With international search report.</i></p>
<p>(54) Title: HUMAN G-PROTEIN CHEMOKINE RECEPTOR HSATU68</p> <p>(57) Abstract</p> <p>Human G-protein chemokine receptor polypeptides and DNA (RNA) encoding such polypeptides and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such polypeptides for identifying antagonists and agonists to such polypeptides and methods of using the agonists and antagonists therapeutically to treat conditions related to the underexpression and overexpression of the G-protein chemokine receptor polypeptides, respectively. Also disclosed are diagnostic methods for detecting a mutation in the G-protein chemokine receptor nucleic acid sequences and detecting a level of the soluble form of the receptors in a sample derived from a host.</p>		



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : C07H 21/04, C12N 1/21, 5/16, 15/12, 15/63, C07K 14/00, C12P 21/00, G01N 33/566	<b>A1</b>	(11) International Publication Number: <b>WO 97/25340</b> (43) International Publication Date: 17 July 1997 (17.07.97)
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(21) International Application Number: PCT/US96/00499

(22) International Filing Date: 11 January 1996 (11.01.96)

(71) Applicant: HUMAN GENOME SCIENCES, INC. [US/US];  
9410 Key West Avenue, Rockville, MD 20850-3338 (US).(72) Inventor: LI, Yi; 16125 Howard Landing Drive, Gaithersburg,  
MD 20878 (US).(74) Agent: BENSON, Robert, H.; Human Genome Sciences, Inc.,  
9410 Key West Avenue, Rockville, MD 20850 (US).(81) Designated States: AU, CA, CN, JP, KR, MX, NZ, US,  
European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR,  
IE, IT, LU, MC, NL, PT, SE).Published  
*With international search report.*

(54) Title: HUMAN G-PROTEIN CHEMOKINE RECEPTOR HSATU68

## (57) Abstract

Human G-protein chemokine receptor polypeptides and DNA (RNA) encoding such polypeptides and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such polypeptides for identifying antagonists and agonists to such polypeptides and methods of using the agonists and antagonists therapeutically to treat conditions related to the underexpression and overexpression of the G-protein chemokine receptor polypeptides, respectively. Also disclosed are diagnostic methods for detecting a mutation in the G-protein chemokine receptor nucleic acid sequences and detecting a level of the soluble form of the receptors in a sample derived from a host.

**FOR THE PURPOSES OF INFORMATION ONLY**

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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 30 APR 1998

WIPO PCT

Applicant's or agent's file reference PF218PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US96/00499	International filing date (day/month/year) 11 JANUARY 1996	Priority date (day/month/year) NONE
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant HUMAN GENOME SCIENCES, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of — sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  01 AUGUST 1997	Date of completion of this report  01 APRIL 1998
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer  MICHAEL PAK <i>[Signature]</i>
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196 <i>for</i>

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US96/00499

## I. Basis of the report

1. This report has been drawn on the basis of (Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments):

- ☒ the international application as originally filed.
- ☒ the description, pages 1-40, as originally filed.  
pages NONE, filed with the demand.  
pages NONE, filed with the letter of \_\_\_\_\_.  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☒ the claims, Nos. 1-28, as originally filed.  
Nos. NONE, as amended under Article 19.  
Nos. NONE, filed with the demand.  
Nos. NONE, filed with the letter of \_\_\_\_\_.  
Nos. \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☒ the drawings, sheets/fig 1-6, as originally filed.  
sheets/fig NONE, filed with the demand.  
sheets/fig NONE, filed with the letter of \_\_\_\_\_.  
sheets/fig \_\_\_\_\_, filed with the letter of \_\_\_\_\_.

2. The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE.
- ☒ the claims, Nos. NONE.
- ☒ the drawings, sheets/fig NONE.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/US96/00499

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 14-20, 23-26, 28

because:

☐ the said international application, or the said claim Nos. \_ relate to the following subject matter which does not require international preliminary examination (*specify*).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_ are so unclear that no meaningful opinion could be formed (*specify*).

☐ the claims, or said claims Nos. \_ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 14-20, 23-26, 28.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US96/00499

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims <u>3, 5-7, 11-13, 21-22, 27</u>	YES
	Claims <u>1-2, 4, 8-10</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-13, 21-22, 27</u>	NO
Industrial Applicability (IA)	Claims <u>1-13, 21-22, 27</u>	YES
	Claims <u>NONE</u>	NO

**2. CITATIONS AND EXPLANATIONS**

Claims 1-2, 4, and 8-10 lack novelty under PCT Article 33(2) as being anticipated by MACHESE et al.

Figure 1A (page 337) discloses the nucleotide and the deduced amino acid sequence of GPR9 which has 99.9% identity with the claimed nucleotide sequence of Figure 1 (of HSATU68) of the application (SEQ ID NO:1) which meets the limitations of claims 1-2 and 8. GPR9 DNA was isolated from genomic library which meets the limitations of claim 4 (page 336, left column). The GPR9 clone was isolated from lambda EMBL3 SP7/T7 vector packaged library which inherently requires the propagation in the bacterial cell which meets the limitations of claims 9-10 (page 336, left column).

Claims 1-2, 4, 8-13, 21-22, and 27 lack an inventive step under PCT Article 33(3) as being obvious over MACHESE et al. in view of SUZUKI et al.

MACHESE et al. teachings are discussed above. MACHESE et al. teach that it is desirable to use binding assays to test which chemokines are functional ligands for the receptor encoded by GPR9 (page 340, left column, middle paragraph; page 344, left column). MACHESE et al. do not disclose a HSATU68 protein.

SUZUKI et al. teach the recombinant expression of IL-8 receptor in CHO cells transfected with IL-8 cDNA in a pRC/CMV vector (page 18265, left column and figure 4). SUZUKI et al. teach the binding assays and competition assays using MGSA, NAP-2, and IL-8 with the transfected CHO cells expressing IL-8 receptor (figures 4 and 6). SUZUKI et al. teach that the N-terminus of IL-8 receptor confers high affinity binding and ligand binding specificity (page 18263, abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the GPR9 DNA of MACHESE et al. to express the GPR9 protein using the expression (Continued on Supplemental Sheet.)

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-4, 8-13, 21-22, and 27 are not fully supported because the description fails to enable practice of the claimed invention. Claims encompass a polypeptide produced with a polynucleotide which results in variants and fragments of polypeptide disclosed in figure 1 with 70% sequence identity. However, the description fails to enable such variant polypeptide because it requires undue experimentation for one skilled in the art to determine whether the variants or fragments are functional. The ligand which activates the claimed G-protein receptor, HSATU68, is not known and without a ligand it would require undue experimentation to test the numerous variants encompassed by the claims. Furthermore, G-protein receptors has seven transmembrane domains which form a pocket for the ligand binding and it is unpredictable to determine effect of mutations in this regions.

**Supplemental B x**

(To be used when the space in any of the preceding boxes is not sufficient)

Sheet 10

Continuation of: Boxes I - VIII

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(6): C07H 21/04; C12N 1/21, 5/16, 15/12, 15/63; C07K 14/00; C12P 21/00; G01N 33/566; and  
US Cl.: 536/23.5, 24.33; 530/350; 435/7.21, 69.1, 252.3, 320.1, 325**V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):**

techniques taught by SUZUKI et al. because MARCHESE et al. teach that it is desirable to use binding assays to test which chemokines are functional ligands for the receptor encoded by GPR9 (page 340, left column, middle paragraph; page 344, left column).

Claim 3 lacks an inventive step under PCT Article 33(3) as being obvious over MARCHESE et al. in view of SAMBROOK et al.

MARCHESE et al. teachings are discussed above. MARCHESE et al. does not teach polynucleotide which is an RNA.

SAMBROOK et al. teach a RNA riboprobes as the probes of choice for most purposes (page 10.3).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the GPR9 DNA of MARCHESE et al. to express make the RNA riboprobe as taught by SAMBROOK et al. One of ordinary skill in the art would have been motivated to make the modification because SAMBROOK et al. teach that RNA riboprobes are superior probes for most purposes.

Claims 5-7 lack an inventive step under PCT Article 33(3) as being obvious over MARCHESE et al.

Figure 1A (page 337) discloses the nucleotide and the deduced amino acid sequence of GPR9 which has 99.9% identity with the claimed nucleotide sequence of Figure 1 (of HSATU68) of the application (SEQ ID NO:1) which meets the limitations of claims 5-7 because the differences are due to obvious allelic variations or due to degeneracy of codon.

Claims 1-13, 21-22, and 27 meet the criteria set out in PCT Article 33(4), because claimed products are useful for generating pharmaceutical compounds.

**NEW CITATIONS**

SAMBROOK et al. Molecular Cloning. New York: Cold Spring Harbor Laboratory Press. 1989, second edition, pages 10.2-10.3 and 10.29-10.35, especially page 10.3.

PCT

TRANSLATION

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference E2437-00	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/JP 96/00499	International filing date (day/month/year) 01.03.96	Priority date (day/month/year) 01.03.95
International Patent Classification (IPC) or national classification and IPC C07C317/14, 317/22, 317/24, 317/44, 323/09, 323/18, 323/22, 323/31, 323/62, A61K31/10, 31/11, 31/12, 31/165, 31/235, 31/275		
Applicant TOYAMA CHEMICAL CO., LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet.
<input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
These annexes consist of a total of _____ sheets.
3. This report contains indications relating to the following items:
I <input checked="" type="checkbox"/> Basis of the report
II <input type="checkbox"/> Priority
III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV <input type="checkbox"/> Lack of unity of the invention
V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement
VI <input type="checkbox"/> Certain documents cited
VII <input type="checkbox"/> Certain defects in the international application
VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 28.06.96	Date of completion of this report 25.03.97
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No.

PCT/J P 9 6 / 0 0 4 9 9

## I. Basis of the report

1. This report has been drawn on the basis of *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*:

- ☒ the international application as originally filed.
- ☐ the description,      pages \_\_\_\_\_, as originally filed,  
    pages \_\_\_\_\_, filed with the demand,  
    pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_,  
    pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☐ the claims,      Nos. \_\_\_\_\_, as originally filed,  
    Nos. \_\_\_\_\_, as amended under Article 19,  
    Nos. \_\_\_\_\_, filed with the demand,  
    Nos. \_\_\_\_\_, filed with the letter of \_\_\_\_\_,  
    Nos. \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☐ the drawings,      sheets/fig \_\_\_\_\_, as originally filed,  
    sheets/fig \_\_\_\_\_, filed with the demand,  
    sheets/fig \_\_\_\_\_, filed with the letter of \_\_\_\_\_,  
    sheets/fig \_\_\_\_\_, filed with the letter of \_\_\_\_\_.

2. The amendments have resulted in the cancellation of:

- ☐ the description,      pages \_\_\_\_\_
- ☐ the claims,      Nos. \_\_\_\_\_
- ☐ the drawings,      sheets/fig \_\_\_\_\_

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/JP 96/00499

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

Novelty (N)	Claims	1-15	YES
	Claims		NO
Inventive step (IS)	Claims	1-15	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-15	YES
	Claims		NO

### 2. Citations and explanations

Neither document [JP, 4-154737, A (OTSUKA PHARMACEUTICAL CO., LTD.), 27 May, 1992 (27.05.92)], nor document [JP, 5-501266, A (United Kingdom), 11 March, 1993 (11.03.93)], nor document [JP, 3-503771, A (MERK PATENT GmbH), 22 August, 1991 (22.08.91)] disclose the compounds defined in the present inventions. In addition, the medicinal effects of the compounds of the present inventions are recognized as mentioned in the description.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/00499

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) : Please See Extra Sheet.

US CL : 536/23.5, 24.33; 530/350; 435/7.21, 69.1, 240.2, 252.3, 320.1;

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.5, 24.33; 530/350; 435/7.21, 69.1, 240.2, 252.3;

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MARCHESE et al. Cloning and Chromosomal Mapping of Three Novel Genes, GPR9, GPR10, and GPR14, Encoding Receptors Related to Interleukin 8, Neuropeptide Y, and Somatostatin Receptors. Genomics. 1995, Vol. 29, pages 335-344, especially pages 337, 340-343.	1-10
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Y		11-13, 21, 22, 27
Y	SUZUKI et al. The N Terminus of Interleukin-8 (IL-8) Receptor Confers High Affinity Binding to Human IL-8. Journal of Biological Chemistry, 15 July 1994, Vol. 269, No. 28, pages 18263-18266, see whole document.	11-13, 21, 22, 27

☐

Further documents are listed in the continuation of Box C.

☐

See patent family annex.

* Special categories of cited documents:	*T*	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be part of particular relevance	*X*	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E* earlier document published on or after the international filing date	*Y*	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Z*	document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means		
*P* document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

16 MAY 1996

Date of mailing of the international search report

06 JUN 1996

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

MICHAEL PAK

Telephone No. (703) 308-0196

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/00499

## B x I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-13, 21-22, 27.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/00499

## A. CLASSIFICATION OF SUBJECT MATTER:

IPC (6):

C07H 21/04; C12N 1/21, 5/16, 15/12, 15/63; C07K 14/00; C12P 21/00; G01N 33/566;

## B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, STN, MEDLINE, CAPLUS, EMBL, GENBANK, GENESEQ, EST-STS, PIR, SWISS-PROT.

search terms: authors, G protein, receptor, glycoprotein, chemokine.

sequence: seq ID # 1, 2, and 9.

## BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1: claims 1-13, 21-22, 27 drawn to human G-protein Chemokine receptor, the DNA encoding it, vector constructs, host cells and method of using the receptor;

Group 2: claim 14 drawn to antibodies;

Group 3: claims 15 and 17 drawn to agonist and method of treatment with agonist;

Group 4: claims 16 and 18 drawn to antagonist and method of treatment with antagonist;

Group 5: claim 19 drawn to a method of human gene therapy;

Group 6: claim 20 drawn to a second method of human gene therapy;

Group 7: claims 23-26 drawn to a method of diagnosis;

Group 8: claim 28 drawn to a second method of diagnosis.

The inventions listed as Groups 1-8 do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons. Group 1 is directed to a receptor, the DNA that encodes it, method of making it, and first method of using the receptor. The special technical feature is the disclosed protein and DNA sequences. Groups 2 and 3 are drawn to structurally different products which do not share the same or a corresponding special technical feature with Group 1. Groups 4-8 are drawn to additional methods with different goals, method steps and starting material, which do not share the same or a corresponding special technical feature with each other or with Groups 1-3. Note that PCT Rule 13 does not provide for multiple products or methods within a single application. Since the special technical feature of each Group invention is not present in any other Group invention, unity of invention is lacking.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US96/00499

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) :Please See Extra Sheet.

US CL :536/23.5, 24.33; 530/350; 435/7.21, 69.1, 240.2, 252.3, 320.1;

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.5, 24.33; 530/350; 435/7.21, 69.1, 240.2, 252.3;

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	MARCHESE et al. Cloning and Chromosomal Mapping of Three Novel Genes, GPR9, GPR10, and GPR14, Encoding Receptors Related to Interleukin 8, Neuropeptide Y, and Somatostatin Receptors. Genomics. 1995, Vol. 29, pages 335-344, especially pages 337, 340-343.	1-10 ----- 11-13, 21, 22, 27
Y	SUZUKI et al. The N Terminus of Interleukin-8 (IL-8) Receptor Confers High Affinity Binding to Human IL-8. Journal of Biological Chemistry, 15 July 1994, Vol. 269, No. 28, pages 18263-18266, see whole document.	11-13, 21, 22, 27



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	*T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be part of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*G* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

16 MAY 1996

Date of mailing of the international search report

06 JUN 1996

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

MICHAEL PAK

Telephone No. (703) 308-0196

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/00499

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-13, 21-22, 27.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

## PATENT COOPERATION TREATY

PCT

NOTIFICATION CONCERNING  
DOCUMENT TRANSMITTED

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

13 October 1997 (13.10.97)

International application No.

PCT/JP96/00499

International filing date (day/month/year)

01 March 1996 (01.03.96)

Applicant

TOYAMA CHEMICAL CO., LTD. et al

The International Bureau transmits herewith the following documents and number thereof:

\_\_\_\_\_ copy of the English translation of the international preliminary examination report (Article 36(3)(a))

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Sean Taylor

Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

BENSON, Robert, H. Esq.  
Human Genome Sciences, Inc.  
9410 Key West Avenue  
Rockville, MD 20850  
ETATS-UNIS D'AMERIQUE

BEST AVAILABLE COPY

Date of mailing (day/month/year) 21 March 1997 (21.03.97)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference PF218PCT	
International application No. PCT/US96/00499	International filing date (day/month/year) 11 January 1996 (11.01.96)

## 1. The following indications appeared on record concerning:

☐ the applicant ☐ the inventor ☒ the agent ☐ the common representative

## Name and Address

SQUIRE, William  
Carella, Byrne, Bain, Gilfillan,  
Cecchi, Stewart & Olstein  
6 Becker Farm Road  
Roseland, NJ 07068  
United States of America

## State of Nationality

## State of Residence

## Telephone No.

## Facsimile No.

## Teleprinter No.

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☒ the person ☒ the name ☒ the address ☐ the nationality ☐ the residence

## Name and Address

BENSON, Robert, H. Esq.  
Human Genome Sciences, Inc.  
9410 Key West Avenue  
Rockville, MD 20850  
United States of America

## State of Nationality

## State of Residence

## Telephone No.

301-309-8504

## Facsimile No.

301-309-8512

## Teleprinter No.

## 3. Further observations, if necessary:

Please also note the change of the agent's file reference number.

## 4. A copy of this notification has been sent to:

☒ the receiving Office ☒ the designated Offices concerned  
☐ the International Searching Authority ☐ the elected Offices concerned  
☐ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

## Authorized officer

G. Bähr

Telephone No.: (41-22) 730.91.11

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 03 October 1997 (03.10.97)	
International application No. PCT/US96/00499	Applicant's or agent's file reference PF218PCT
International filing date (day/month/year) 11 January 1996 (11.01.96)	Priority date (day/month/year)
Applicant HUMAN GENOME SCIENCES, INC. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

01 August 1997 (01.08.97)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

BEST AVAILABLE COPY

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Jocelyne Rey-Millet Telephone No.: (41-22) 338.83.38
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## TENT COOPERATION TREATY

**PCT****NOTIFICATION REGARDING THE  
CONFIRMATION OF PRECAUTIONARY  
DESIGNATIONS**

(PCT Rule 24.2(a), last sentence)

From the INTERNATIONAL BUREAU

To:

BENSON, Robert, H.  
Human Genome Sciences, Inc.  
9410 Key West Avenue  
Rockville, MD 20850  
ETATS-UNIS D'AMERIQUE

Date of mailing ( <i>day/month/year</i> ) 18 July 1997 (18.07.1997)		
Applicant's or agent's file reference PF218PCT		<b>IMPORTANT NOTIFICATION</b>
International application No. PCT/US96/00499	International filing date ( <i>day/month/year</i> ) 11 January 1996 (11.01.1996)	Priority date ( <i>day/month/year</i> )
Applicant HUMAN GENOME SCIENCES, INC.		

1. The applicant is hereby notified that, pursuant to the confirmation of precautionary designations, the following designated Offices will also be notified of the receipt of the record copy by the International Bureau:

List of designated Offices :  
National: US

Name(s) of applicant(s) for  
the designated States concerned : LI, Yi

2. This notification complements the Notification of Receipt of Record Copy (Form PCT/IB/301).
3. The applicant is reminded that:
- (i) the data appearing above, and especially the (list of) designation(s) should be carefully checked;
  - (ii) the time limits for entering the national phase in the designated Offices must be monitored by the applicant (see the Annex to Form PCT/IB/301).
4. A copy of this notification is being sent to the receiving Office.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer G. Bähr
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

## PATENT COOPERATION TREATY

PCT

COMMUNICATION OF  
INTERNATIONAL APPLICATIONS

(PCT Article 20)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ETATS-UNIS D'AMERIQUE

Date of mailing:

12 September 1997 (12.09.97)

in its capacity as designated Office

The International Bureau transmits herewith copies of the international applications having the following international application numbers and international publication numbers:

International application no.:

PCT/US96/00499

International publication no.:

WO97/25340

**CORRECTED VERSION  
VERSION CORRIGEE**

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer:

J. Zahra  
Telephone No.: (41-22) 338.83.38

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/00499

## A. CLASSIFICATION OF SUBJECT MATTER: IPC (6):

C07H 21/04; C12N 1/21, 5/16, 15/12, 15/63; C07K 14/00; C12P 21/00; G01N 33/566;

## B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, STN, MEDLINE, CAPLUS, EMBL, GENBANK, GENESEQ, EST-STS, PIR, SWISS-PROT.  
search terms: authors, G protein, receptor, glycoprotein, chemokine.  
sequence: seq ID # 1, 2, and 9.

## BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1: claims 1-13, 21-22, 27 drawn to human G-protein Chemokine receptor, the DNA encoding it, vector constructs, host cells and method of using the receptor;

Group 2: claim 14 drawn to antibodies;

Group 3: claims 15 and 17 drawn to agonist and method of treatment with agonist;

Group 4: claims 16 and 18 drawn to antagonist and method of treatment with antagonist;

Group 5: claim 19 drawn to a method of human gene therapy;

Group 6: claim 20 drawn to a second method of human gene therapy;

Group 7: claims 23-26 drawn to a method of diagnosis;

Group 8: claim 28 drawn to a second method of diagnosis.

The inventions listed as Groups 1-8 do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons. Group 1 is directed to a receptor, the DNA that encodes it, method of making it, and first method of using the receptor. The special technical feature is the disclosed protein and DNA sequences. Groups 2 and 3 are drawn to structurally different products which do not share the same or a corresponding special technical feature with Group 1. Groups 4-8 are drawn to additional methods with different goals, method steps and starting material, which do not share the same or a corresponding special technical feature with each other or with Groups 1-3. Note that PCT Rule 13 does not provide for multiple products or methods within a single application. Since the special technical feature of each Group invention is not present in any other Group invention, unity of invention is lacking.